

**PATENT COOPERATION TREATY**

From the  
**INTERNATIONAL SEARCHING AUTHORITY**

REC'D 27 APR 2005

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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

**25 APR 2005**

Applicant's or agent's file reference  PU60525		Date of mailing (day/month/year)  FOR FURTHER ACTION See paragraph 2 below
International application No.  PCT/US04/32824	International filing date (day/month/year)  06 October 2004 (06.10.2004)	Priority date (day/month/year)  06 October 2003 (06.10.2003)
International Patent Classification (IPC) or both national classification and IPC  IPC(7): A61K 31/437; C07D 471/04; A61P 9/00 and US Cl.: 514/303; 546/118		
Applicant  GLAXO GROUP LIMITED		

1. This opinion contains indications relating to the following items:

<input checked="" type="checkbox"/>	Box No. I	Basis of the opinion
<input type="checkbox"/>	Box No. II	Priority
<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
<input type="checkbox"/>	Box No. IV	Lack of unity of invention
<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
<input type="checkbox"/>	Box No. VI	Certain documents cited
<input type="checkbox"/>	Box No. VII	Certain defects in the international application
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application

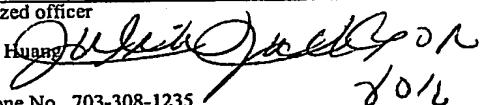
2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US  Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer  Evelyn Huang  Telephone No. 703-308-1235 8016
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/32824

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

a sequence listing  
 table(s) related to the sequence listing

b. format of material

in written format  
 in computer readable form

c. time of filing/furnishing

contained in international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.

3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/32824

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims 2	YES
	Claims 1, 3-7	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-7	NO
Industrial applicability (IA)	Claims 1-7	YES
	Claims NONE	NO

**2. Citations and explanations:**

Claims 1, 3-7 lack novelty under PCT Article 33(2) as being anticipated by BAILEY et al. The Rho kinase inhibiting compounds described in the abstract, its composition and method of use, are encompassed by the instant claims wherein R1 is ethyl, cyclopropyl, or phenyl, X is O, S or NH, R2 is methyl or optionally substituted phenyl.

Claim 2 lack an inventive step under PCT Article 33(3) as being obvious over BAILEY et al. The Rho kinase inhibiting compounds described in the abstract with RN 607373-93-3 has an ethyl whereas the instant compound on page 122, lines 11-12 has a phenyl as R1. Ethyl and phenyl, however, are optional choices for R1 (corresponding to R2 in BAILEY et al). One of ordinary skill in the art would be motivated to replace the ethyl with the alternative phenyl to arrive at the instant invention.

Claim 2 meet the criteria set out in PCT Article 33(2), because the prior art does not specifically describe the compounds in the instant claim 2.

Claims 1-7 meet the criteria set out in PCT Article 33(4), and thus find industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry as a therapeutic agent for treating a disorder associated with inappropriate Rho kinase activity.